Amendment to the Specification:

- Please delete paragraph [0084] and replace it with the following paragraph:

[0084] In preferred embodiments the targeting element binds to an epitope on pIgR or the pIgR stalk that comprises an amino acid sequence selected from the following: LRKED **(SEQ ID NO: 37)**, QLFVNEE **(SEQ ID NO: 38)**, LNQLT **(SEQ ID NO: 39)**, YWCKW **(SEQ ID NO: 40)**, GWYWC **(SEQ ID NO: 41)**, STLVPL **(SEQ ID NO: 42)**, SYRTD **(SEQ ID NO: 43)**, QDPRLF **(SEQ ID NO: 44)** and KRSSK **(SEQ ID NO: 45)**. In more preferred embodiments the targeting element binds to pIgR or the pIgR stalk in a region selected from the following:

R1 KRSSK **(SEQ ID NO: 45)** to the carboxy terminus of pIgR;

R2a From SYRTD **(SEQ ID NO: 43)** to the carboxy terminus of pIgR,

R2b From SYRTD **(SEQ ID NO: 43)** to KRSSK **(SEQ ID NO: 45)**,

R3a From STLVPL **(SEQ ID NO: 42)** to the carboxy terminus of pIgR,

R3b From STLVPL **(SEQ ID NO: 42)** to KRSSK **(SEQ ID NO: 45)**,

R3c From STLVPL **(SEQ ID NO: 42)** to SYRTD **(SEQ ID NO: 43)**,

R4a From GWYWC **(SEQ ID NO: 41)** to the carboxy terminus of pIgR,

R4b From GWYWC **(SEQ ID NO: 41)** to KRSSK **(SEQ ID NO: 45)**,

R4c From GWYWC **(SEQ ID NO: 41)** to SYRTD **(SEQ ID NO: 43)**,

R4d From GWYWC **(SEQ ID NO: 41)** to STLVPL **(SEQ ID NO: 42)**,

R5a From YWCKW **(SEQ ID NO: 40)** to the carboxy terminus of pIgR,

R5b From YWCKW **(SEQ ID NO: 40)** to KRSSK **(SEQ ID NO: 45)**,

R5c From YWCKW **(SEQ ID NO: 40)** to SYRTD **(SEQ ID NO: 43)**,

R5d From YWCKW **(SEQ ID NO: 40)** to STLVPL **(SEQ ID NO: 42)**,

R5e From YWCKW **(SEQ ID NO: 40)** to GWYWC **(SEQ ID NO: 41)**,

R6a From LNQLT **(SEQ ID NO: 39)** to the carboxy terminus of pIgR,

R6b From LNQLT **(SEQ ID NO: 39)** to KRSSK **(SEQ ID NO: 45)**,

R6c From LNQLT **(SEQ ID NO: 39)** to SYRTD **(SEQ ID NO: 43)**,

R6d From LNQLT **(SEQ ID NO: 39)** to STLVPL **(SEQ ID NO: 42)**,

R6e From LNQLT **(SEQ ID NO: 39)** to GWYWC **(SEQ ID NO: 41)**,

R6f From LNQLT **(SEQ ID NO: 39)** to YWCKW **(SEQ ID NO: 40)**,

R7a From QLFVNEE **(SEQ ID NO: 38)** to the carboxy terminus of pIgR,

R7b From QLFVNEE **(SEQ ID NO: 38)** to KRSSK **(SEQ ID NO: 45)**,

R7c From QLFVNEE **(SEQ ID NO: 38)** to SYRTD **(SEQ ID NO: 43)**,

R7d From QLFVNEE **(SEQ ID NO: 38)** to STLVPL **(SEQ ID NO: 42)**,

R7e From QLFVNEE **(SEQ ID NO: 38)** to GWYWC **(SEQ ID NO: 41)**,

R7f From QLFVNEE **(SEQ ID NO: 38)** to YWCKW **(SEQ ID NO: 40)**,

R7g From QLFVNEE **(SEQ ID NO: 38)** to LNQLT **(SEQ ID NO: 39)**,

R8a From LRKED **(SEQ ID NO: 37)** to the carboxy terminus of pIgR,

R8b From LRKED **(SEQ ID NO: 37)** to KRSSK **(SEQ ID NO: 45)**,

R8c From LRKED **(SEQ ID NO: 37)** to SYRTD **(SEQ ID NO: 43)**,

R8d From LRKED **(SEQ ID NO: 37)** to STLVPL **(SEQ ID NO: 42)**,

R8e From LRKED **(SEQ ID NO: 37)** to GWYWC **(SEQ ID NO: 41)**,

R8f From LRKED **(SEQ ID NO: 37)** to YWCKW **(SEQ ID NO: 40)**,

R8g From LRKED **(SEQ ID NO: 37)** to LNQLT **(SEQ ID NO: 39)**, and

R8h From LRKED **(SEQ ID NO: 37)** to QLFVNEE. **(SEQ ID NO: 38)**

- Please delete paragraph [0090] and replace it with the following paragraph:

[0090] Figure 1 provides a schematic illustration of an sFv domain structure, and a model of the interactions between sFvs forming a dimeric "diabody" structure. **Peptide fragments shown in SEQ ID NOS 46, 49 & 52.**

- Please delete paragraph [0094] and replace it with the following paragraph:

[0094] Figure 5 depicts the coding sequence **(SEQ ID NO: 53)** of an exemplary pIgR-directed sFv (APL10).

- Please delete paragraph [0095] and replace it with the following paragraph:

[0095] Figure 6 depicts the coding sequence **(SEQ ID NO: 54)** of an exemplary pIgR-directed sFv-IL-2 fusion protein.

- Please delete paragraph [0096] and replace it with the following paragraph:

[0096] Figure 7 provides maps of exemplary IL-2-sFv expression constructs. **Peptide fragments shown in SEQ ID NOS 50 & 51.**

- Please delete paragraph [0196] and replace it with the following paragraph:

[0196] Various amino acid sequences are known that may serve as suitable spacers in the compounds of the invention (for a review, see Simons, Spacers, probability, and yields, Bioconjug Chem 1999 Jan-Feb;10(1):3-8). Some non-limiting examples of sequences that have been used in sFvs include EGKSSGSGSESKEF (SEQ ID NO: 10), one or more copies of GGGGS [also known as $(G_4S)_x$ **(SEQ ID NO: 46)**] (Newton *et al.*, Angiogenin single-chain immunofusions: influence of peptide linkers and spacers between fusion protein domains, Biochemistry 1996 Jan 16;35(2):545-53), GSGS [also known as $(GSGS)_x$ **(SEQ ID NO: 47)**] and GSSG [also known as $(GSSG)_x$ **(SEQ ID NO: 48)**].

- Please delete paragraph [0211] and replace it with the following paragraph:

[0211] The PCR product from the overlap PCR was gel purified and cloned directly into the mammalian expression vector pcDNA3.1D/V5-His-TOPO® expression vector (Invitrogen, Carlsbad, CA). This expression vector includes a CMV-derived promoter for high-level, constitutive expression; a C-terminal V5 epitope tag that can be detected with anti-V5 antibody; and a further C-terminal 6xHis tag **(SEQ ID NO: 49)** that can be detected with an anti-6xHis tag **(SEQ ID NO: 49)** antibody or used to purify the IL-2-5A fusion protein. Anti-V5 and anti-6xHis **(SEQ ID NO: 49)** antibodies are available from Invitrogen.

- Please delete paragraph [0217] and replace it with the following paragraph:

[0217] IMAC chromatography was used to purify IL-2-sFv fusion protein from transiently transfected cells. In brief, about 400 ml of media from transfected COS-1 cells incubated for 48 to 144 hours was harvested. The media was pooled and Imidazole was added to a final concentration of 10 mM. A Pellicon cassette System (Millipore Bioscience, Bedford, MA) was used to concentrate the pool to a final volume of ~75 ml. The concentrated sample was then purified using a nickel column, to which the 6xHis tag **(SEQ ID NO: 49)** binds.

- Please delete paragraph [0219] and replace it with the following paragraph:

[0219] A Carboxy terminal fusion of IL-2 with a pIgR-directed sFv designed to favor dimeric sFv formation was constructed by cloning IL-2 without its signal peptide into the AvrII site of the sFv depicted in Fig. 5. A linker comprising of $(Gly_3\ Ser)_2$ **(SEQ ID NO: 50)** was included in the 5' oligonucleotides and two Stop codons were included in the 3' oligonucleotides.

- Please delete paragraph [0235] and replace it with the following paragraph:

[0235] An amino terminal fusion of IL-2 with an sFv designed to favor sFv dimer formation was constructed by cloning IL-2, with its signal peptide, into the Nhe1 site of the sFv shown in Fig. 5. A linker consisting of $(Gly_2Ser)_2$ **(SEQ ID NO: 51)** had previously been ligated to the 5' end of this sFv.

- Please delete paragraph [0237] and replace it with the following paragraph:

[0237] Twenty five cycles of PCR were performed at 58°C. The PCR product was cloned into an intermediate vector: pCR-BluntII-TOPO (Invitrogen, Carlsbad, CA). The IL-2 PCR product was cut out from this intermediate vector using EcoRV and Nhe1, gel purified and

cloned into the Nhe1 site of $(Gly_2Ser)_2$ **(SEQ ID NO: 51)**-sFv in the mammalian expression vector pDIZ. pDIZ was constructed as follows: A 4882bp Spe1/EcoRV fragment was isolated from pcDNA 3.1 Hygro (Invitrogen, CA) and ligated to a Spe1/Xmn1 fragment from gWiz (Gene Therapy Systems Inc.). A plasmid map of pDIZ is shown in Fig. 7.

- Please delete paragraph [0248] and replace it with the following paragraph:

[0248] The forward primer used to generate the α-IFN 544 bp PCR product was designed to include sequences encoding a synthetic linker encoding 5 amino acids (Gly-Gly-Gly-Gly-Ser) **(SEQ ID NO: 46)** that are connected in frame to the C-terminus sFv polypeptide. The 3-step PCR amplification reaction included 5 cycles with annealing temperature at 55°C followed by 30 cycles at 60°C. The 544 bp PCR product was gel purified and cloned into the pCR Blunt II TOPO intermediate vector. Miniprep DNA was made and positives clones verified for the PCR product by DNA sequencing. Following sequence confirmation, the PCR product was excised by digesting the maxiprep DNA with AvrII and SalI restriction enzymes, then ligated into AvrII / SalI digested APL-10 pELK vector DNA using T4 DNA ligase. Miniprep DNA was prepared and positive clones confirmed by DNA sequencing. Positive vector clones are illustrated in Figure 1 and contain the chimeric DNA sequence (SEQ ID NO: 18) which encodes a chimeric protein containing the following protein domain structural orientation: (NH_2)-pel-B leader-sFv-Gly_4Ser linker-α-IFN -(COOH). **Linker shown in SEQ ID NO: 46.**

- Please delete paragraph [0256] and replace it with the following paragraph:

[0256] The forward primer used to generate the partial APL-10-□-IFN 551 bp PCR product was designed to include sequences encoding a synthetic linker encoding 5 amino acids (Gly-Gly-Gly-Gly-Ser) **(SEQ ID NO: 46)** that can be inserted in frame to the C-terminus of sFv polypeptide APL-10. The 3-step PCR amplification reaction included 5

cycles with annealing temperature at 55°C followed by 30 cycles at 60°C. The 551 bp PCR product was QIAquick column purified and cloned into the pCR Blunt II TOPO intermediate vector. Miniprep DNA was made and positives clones verified by DNA sequencing. Following sequence confirmation, the PCR product was inserted into the AvrII / SalI sites of APL-10E vector (pELK vector derivative), or AvrII / XhoI digested APL-2005S vector (pSyn vector derivative) DNAs. Miniprep DNA was prepared and positive clones confirmed by DNA sequencing. Positive vector clones are illustrated in Figure 2 and contain the chimeric DNA sequence (SEQ ID NO: 24) which encode for a chimeric protein containing the following domains and oriented from the N-terminus: (NH_2)-pel-B leader-sFv-Gly_4Ser linker-β-IFN-(COOH). **Linker shown in SEQ ID NO: 46.**

sFv-β-IFN chimera DNA sequence (SEQ ID NO: 24):

```
ATGAAATACC TATTGCCTAC GGCAGCCGCT GGATTGTTAT TACTCGCGGC CCAGCCGGCC   60
ATGGCCCAGG TGCAGCTGCA GCAATCAGGG GGAGGCGTGG TCCAGCCTGG GAGGTCCCTG  120
AGACTCTCCT GTGCAGCCTC TGGATTCACC TTCAGTAGCT ATGCTATGCA CTGGGTCCGC  180
CAGGCTCCAG GGAAGGGGCT GGAGTGGGTC TCAGCTATTA GTGGTAGTGG TGGTAGCACA  240
TACTACGCAG ACTCCGTGAA GGGCCGGTTC ACCATCTCCA GAGACAACGC CAAGAACTCA  300
CTGTATCTGC AAATGAACAG CCTGAGAGCC GAGGACACGG CTGTGTATTA CTGTGCGAGA  360
GATACCCGAG GGTACTTCGA TCTCTGGGGC CGTGGCACCC TGGTCACCGT CTCCTCAGGT  420
GGCGGAGGGT CATCTGAGCT GACTCAGGAC CCTGCTATGT CTGTGGCCTT GGGACAGACA  480
GTCAGAATCA CATGTCAAGG GGACAGTCTC AGAAAGTATC ATGCAAGCTG GTATCAGCAG  540
AAGCCAGGGC AGGCCCCTGT TCTTGTCATC TATGGTAAGA ATGAACGTCC CTCAGGGATC  600
CCAGAGCGAT TCTCTGGGTC CACCTCAGGA GACACAGCTT CCTTGACCAT CAGTGGGCTC  660
CAGGCGGAAG ATGAGGCTGA CTATTACTGT CACTCCCGAG ACTCTAATGC TGATCTTGTG  720
GTGTTCGGCG GAGGGACCAA GGTCACCGTC CTAGGTGGTG GCGGAGGGTC AATGAGCTAC  780
AACTTGCTTG GATTCCTACA AAGAAGCAGC AATTTTCAGT GTCAGAAGCT CCTGTGGCAA  840
TTGAATGGGA GGCTTGAATA CTGCCTCAAG GACAGGATGA ACTTTGACAT CCCTGAGGAG  900
ATTAAGCAGC TGCAGCAGTT CCAGAAGGAG GACGCCGCAT TGACCATCTA TGAGATGCTC  960
CAGAACATCT TTGCTATTTT CAGACAAGAT TCATCTAGCA CTGGCTGGAA TGAGACTATT 1020
GTTGAGAACC TCCTGGCTAA TGTCTATCAT CAGATAAACC ATCTGAAGAC AGTCCTGGAA 1080
GAAAAACTGG AGAAAGAAGA TTTCACCAGG GGAAAACTCA TGAGCAGTCT GCACCTGAAA 1140
AGATATTATG GGAGGATTCT GCATTACCTG AAGGCCAAGG AGTACAGTCA CTGTGCCTGG 1200
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ACCATAGTCA GAGTGGAAAT CCTAAGGAAC TTTTACTTCA TTAACAGACT TACAGGTTAC 1260
CTCCGAAACT AA 1272

- Please delete paragraph [0258] and replace it with the following paragraph:

[0258] The IFNβ region was amplified by PCR using primers MG sigP(-)HIFNβ 5' (SEQ ID NO:27) and MG HIFNβ 3' (SEQ ID NO:28) and pDIZ HIFNβ-APL10 as a template. The wild-type signal peptide was removed and replaced with a (Gly-Gly-Gly-Ser)x2 linker **(SEQ ID NO: 50)**. The signal peptide minus HIFNβ PCR product was digested with AvrII and NotI and inserted into pgWIZtpaSigP-APL10 cut with the same enzymes to make pgWIZtpaSigP-APL10-HIFNβ. The resulting products were screened by miniprep and verified by sequencing. To subclone the tpaSigP-APL10-HIFNβ into pDIZ, pgWIZtpaSigP-APL10-HIFNβ was cut with EcoRV and NotI and the tpaSigP-APL10-HIFNβ fragment was gel purified.

MG sigP(-)HIFNβ 5' (SEQ ID NO:27):

5'- GTCCTAGGTGGCGGCGGAAGCGGCGGAGGCTCCATGAGCTACAACTTGCTTGGATTCCTAC

AAAGAAGCAGCA -3'

MG HIFNβ 3' (SEQ ID NO:28)

5'- TGCGGCCGCTTAGCTAGCTTATTAGTTTCGGAGGTAACCTGTAAGTCTGTTAATGAAGTAA

AAGTTCCT -3'

The tpaSigP-APL10-HIFNβ fragment was inserted into pDIZ cut with EcoRV and NotI to make pDIZtpaSigP-APL10-HIFNβ. The full-length insert was sequenced and verified to be correct.

TPA SigP-APL10-IFNβ (SEQ ID NO: 29):

ATGGATGCAA TGAAGAGAGG GCTCTGCTGT GTGCTGCTGC TGTGTGGAGC AGTCTTCGTT ~~50~~ **60**
TCGCCCAGCC AGGTACAGCT GCAGCAATCA GGGGGAGGCG TGGTCCAGCC TGGGAGGTCC ~~100~~ **120**
CTGAGACTCT CCTGTGCAGC CTCTGGATTC ACCTTCAGTA GCTATGCTAT GCACTGGGTC ~~150~~ **180**
CGCCAGGCTC CAGGGAAGGG GCTGGAGTGG GTCTCAGCTA TTAGTGGTAG TGGTGGTAGC ~~200~~ **240**
ACATACTACG CAGACTCCGT GAAGGGCCGG TTCACCATCT CCAGAGACAA CGCCAAGAAC ~~250~~ **300**
TCACTGTATC TGCAAATGAA CAGCCTGAGA GCCGAGGACA CGGCTGTGTA TTACTGTGCG ~~300~~ **360**
AGAGATACCC GAGGGTACTT CGATCTCTGG GGCCGTGGCA CCCTGGTCAC CGTCTCCTCA ~~350~~ **420**
GGTGGCGGAG GGTCATCTGA GCTGACTCAG GACCCTGCTA TGTCTGTGGC CTTGGGACAG ~~400~~ **480**
ACAGTCAGAA TCACATGTCA AGGGGACAGT CTCAGAAAGT ATCATGCAAG CTGGTATCAG ~~450~~ **540**
CAGAAGCCAG GGCAGGCCCC TGTTCTTGTC ATCTATGGTA AGAATGAACG TCCCTCAGGG ~~500~~ **600**
ATCCCAGAGC GATTCTCTGG GTCCACCTCA GGAGACACAG CTTCCTTGAC CATCAGTGGG ~~550~~ **660**
CTCCAGGCGG AAGATGAGGC TGACTATTAC TGTCACTCCC GAGACTCTAA TGCTGATCTT ~~600~~ **720**
GTGGTGTTCG GCGGAGGGAC CAAGGTCACC GTCCTAGGTG GCGGCGGAAG CGGCGGAGGC ~~650~~ **780**
TCCATGAGCT ACAACTTGCT TGGATTCCTA CAAAGAAGCA GCAATTTTCA GTGTCAGAAG ~~700~~ **840**
CTCCTGTGGC AATTGAATGG GAGGCTTGAA TACTGCCTCA AGGACAGGAT GAACTTTGAC ~~750~~ **900**
ATCCCTGAGG AGATTAAGCA GCTGCAGCAG TTCCAGAAGG AGGACGCCGC ATTGACCATC ~~800~~ **960**
TATGAGATGC TCCAGAACAT CTTTGCTATT TTCAGACAAG ATTCATCTAG CACTGGCTGG ~~850~~ **1020**
AATGAGACTA TTGTTGAGAA CCTCCTGGCT AATGTCTATC ATCAGATAAA CCATCTGAAG ~~900~~ **1080**
ACAGTCCTGG AAGAAAAACT GGAGAAAGAA GATTTCACCA GGGGAAAACT CATGAGCAGT ~~950~~ **1140**
CTGCACCTGA AAAGATATTA TGGGAGGATT CTGCATTACC TGAAGGCCAA GGAGTACAGT ~~1000~~ **1200**
CACTGTGCCT GGACCATAGT CAGAGTGGAA ATCCTAAGGA ACTTTTACTT CATTAACAGA ~~1050~~ **1260**
CTTACAGGTT ACCTCCGAAA CTAA ~~1074~~**1284**

- Please delete paragraph [0268] and replace it with the following paragraph:

[0268] Figure 1 shows the schematic structure of the sFv directed to a pIgR epitope used for the following *in vivo* transport studies. Indicated are the Pelb leader (a leader sequence that directs secretion from *E. coli*); linker (amino acid sequence $(gly\text{-}gly\text{-}gly\text{-}gly\text{-}ser)_n$)**(SEQ ID NO: 46)**; H_6, (6xHis tag) **(SEQ ID NO: 49)**; cysteine tag (amino acid sequence gly-gly-gly-gly-cys) **(SEQ ID NO: 52)**; and the heavy and light chains of the sFv. The selected sFv comprises an altered FR2 region, an internal unpaired cysteine, a C-terminal His tag, and a single linker repeat. This construct directs near homogenous dimeric sFv formation.

- Between pages 88-89, on a separate page, please insert the Sequence Listing submitted herewith.